Acute Kidney Injury

Amandeep Khurana, MD
Clinical Assistant Professor, Univ of Arizona
Transplant Nephrologist, Southwest Kidney Institute

66 yr white male w/ DM, HTN, CAD admitted to an OSH w/ E Coli UTI, developed E Coli bacteremia and Shock (on vaso + levo) transferred to BUMC w/

- No UO x 12 hrs (despite IVF)
- Cr 1 (baseline 0.9)

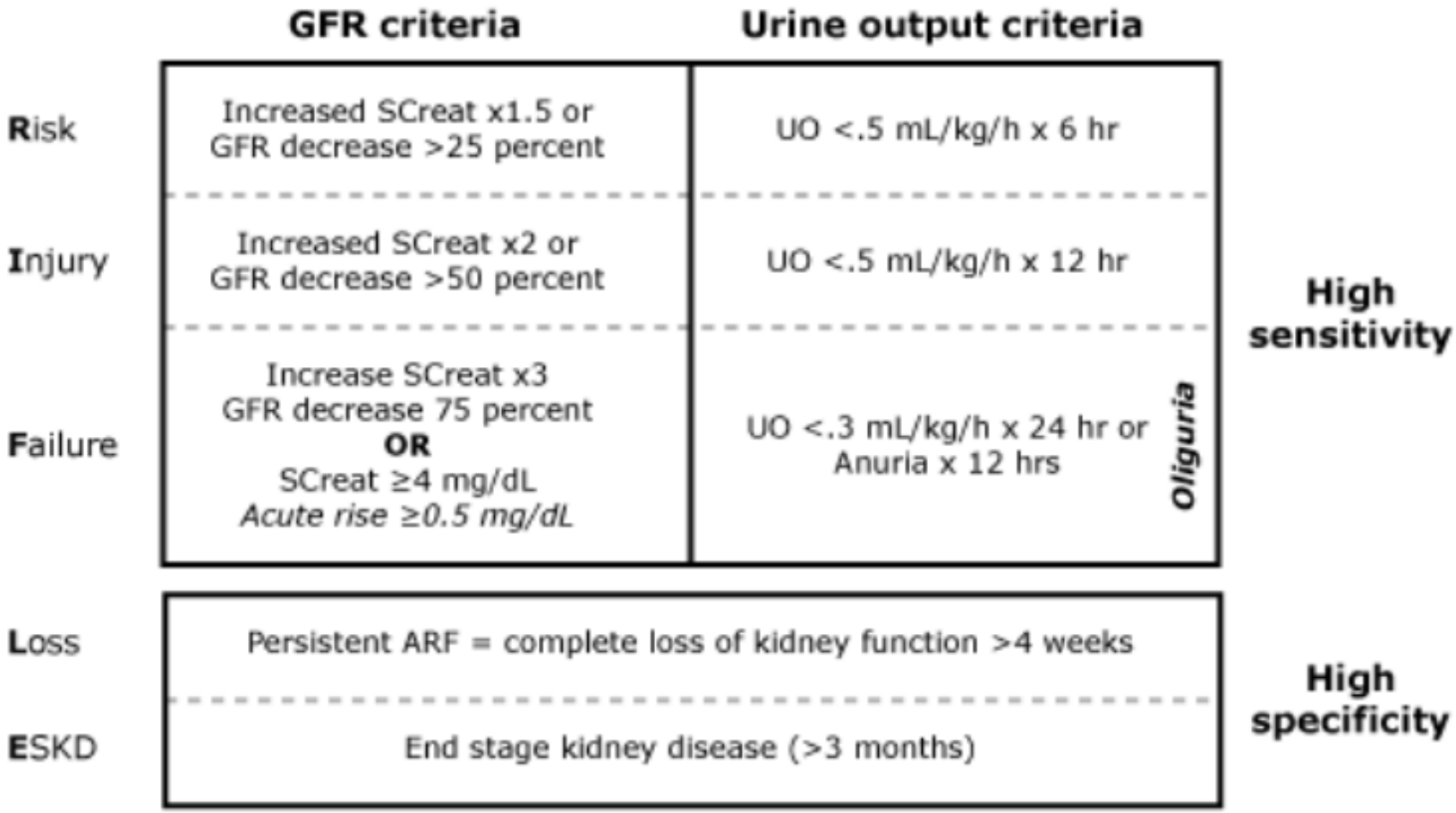
Does this patient have AKI?

A. No, the Cr is unchanged
B. Yes, the patient is oligoanuric
C. Unclear, will have to monitor for now

What is AKI?

- abrupt (within 48 hours)
- absolute increase in Cr of ≥0.3 mg/dL
- increase in Cr of ≥50 percent
- oliguria of (< 0.5 mL/kg/hr) X >6 hrs

Caveats
1. only after volume status had been optimized
2. Urinary tract obstruction to be excluded (if oliguria was sole diagnostic criterion)



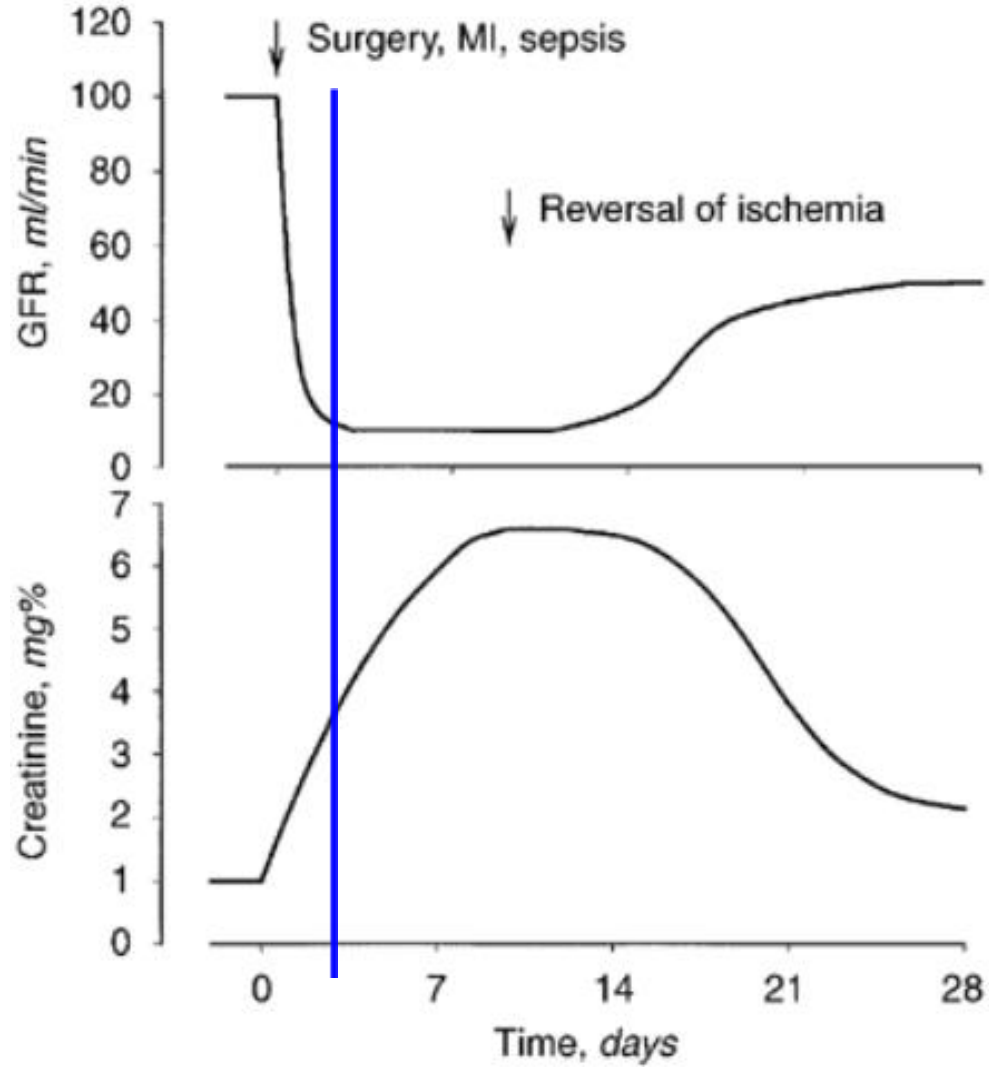
Bellomo, R, Ronco, C, Kellum, JA, et al. Acute renal failure-definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8:B204.

64 yr AAM w/ DM, HTN, CAD, baseline Cr = 0.9 undergo CABG. His post-op Cr:

Day #1 = 2
Day #2 = 3
Day #4 = 4
Day #5 = 5

Is his kidney function getting worse from day 2 to day 5?

A. Yes
B. No


120
100
80
60
40
20
0
GFR, ml/min
Surgery, MI, sepsis
Reversal of ischemia
7
6
5
4
3
2
1
0
Creatinine, mg%
0
7
14
21
28
Time, days

64 yr twins w/ DM, HTN, CAD, baseline Cr = 0.9 undergo CABG. On post-op day #1,

Twin A: Cr = 1.5 (otherwise completely stable)

Twin B: Cr = 0.9 (otherwise completely stable)

A. AKI does not change mortality risk
B. They’re both stable, their mortality risk is the same
C. Twin A is more likely to die
D. Twin B is more likely to die

Twin A is more likely to die. But, how much more likely?

A. 10% more likely to die
B. 25% more likely to die
C. 75% more likely to die
D. 400% more likely to die

Variables	≤25% Decrease in eGFR (n=2631)	>25% Decrease in eGFR or Dialysis (n=829)	>50% Decrease in eGFR or Dialysis (n=228)	>75% Decrease in eGFR or Dialysis (n=119)
Median hospital length of stay, d (Q1, Q3)*	7 (5, 9)	10 (6, 17)	14 (7, 27)	19 (6, 36)
Mortality rates				
n (%)	25 (1.0%)	83 (10%)	58 (25%)	46 (39%)
Unadjusted OR (95% CI)	Reference	11.6 (7.4–18.3)	21.7 (14.4–32.6)	33.3 (21.3–52.0)
Adjusted OR (95% CI)†	Reference	4.0 (2.3–6.7)	5.9 (3.6–9.8)	9.5 (5.4–16.9)

Karkouti et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. Circulation. 2009 Feb 3;119(4):495-502

25 yr male without any PMH goes for a hike. He presents to the ER w/ AKI (Cr 2).

The FeNa is < 1%.

What's the specificity of FeNa < 1% in diagnosis of pre-renal AKI?

A. 34%
B. 52%
C. 78%
D. 90%

FeNa. what is it really good for?

FENa < 1 indicates pre-renal azotemia

	Pre-renal azotemia	ATN (oliguric and non-oliguric)
FENa < 1	27	4
FENa > 1	3	51

Sensitivity: 90%

Specificity: 93%

FENa > 1 indicates ATN

	Pre-renal azotemia	ATN (oliguric and non-oliguric)
FENa > 1	3	51
FENa < 1	27	4

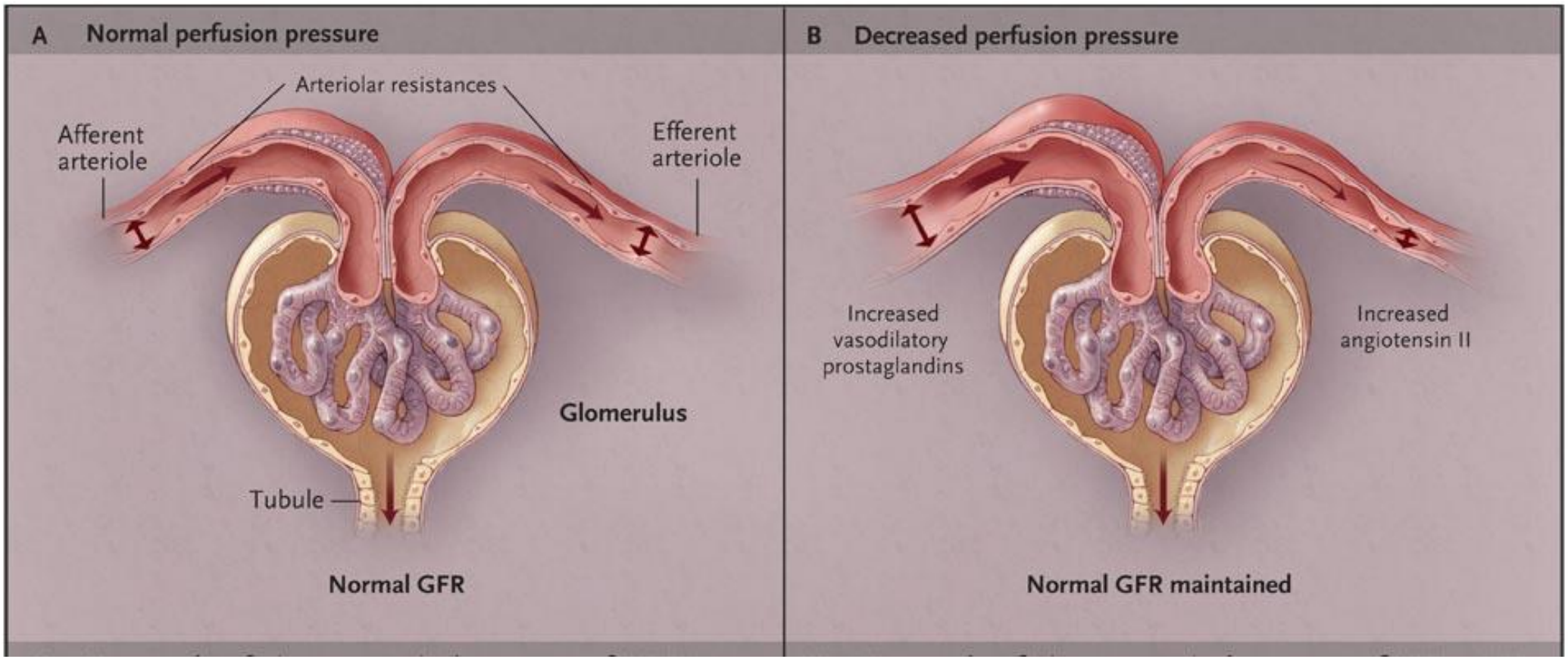
Sensitivity: 93%

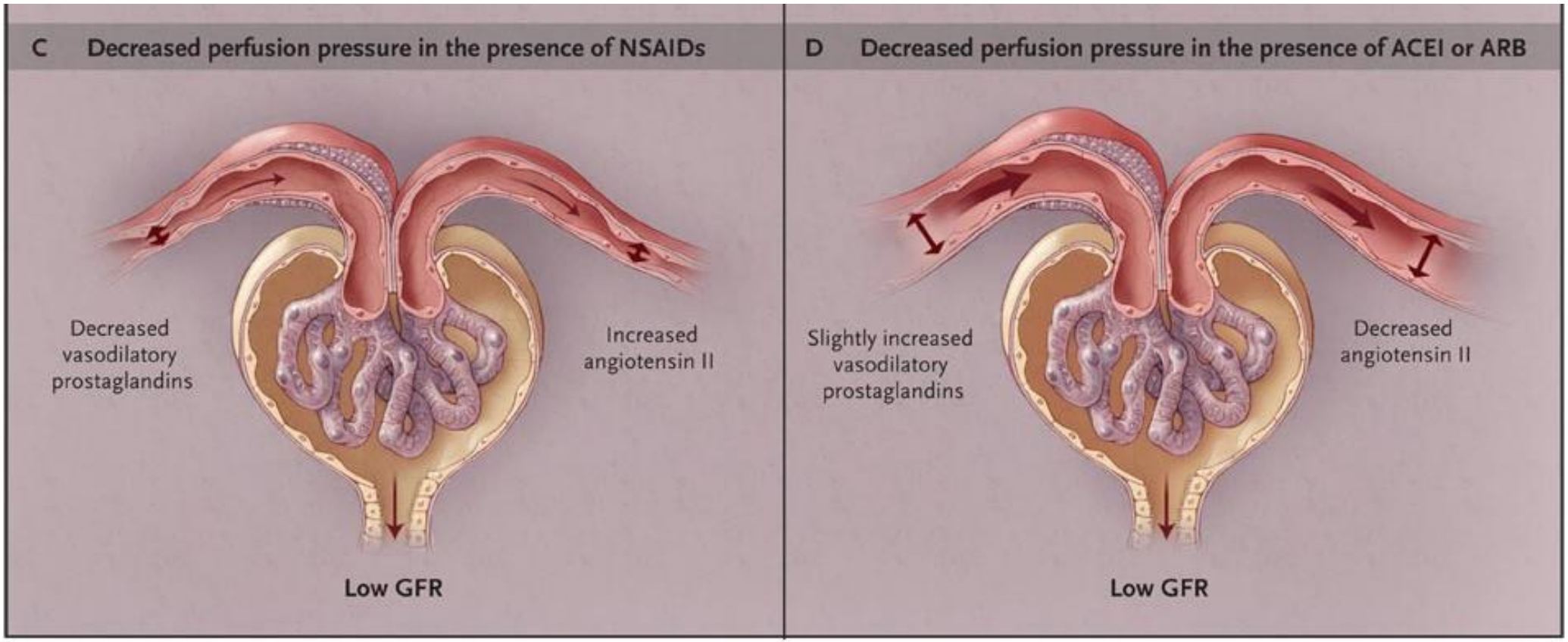
Specificity: 90%

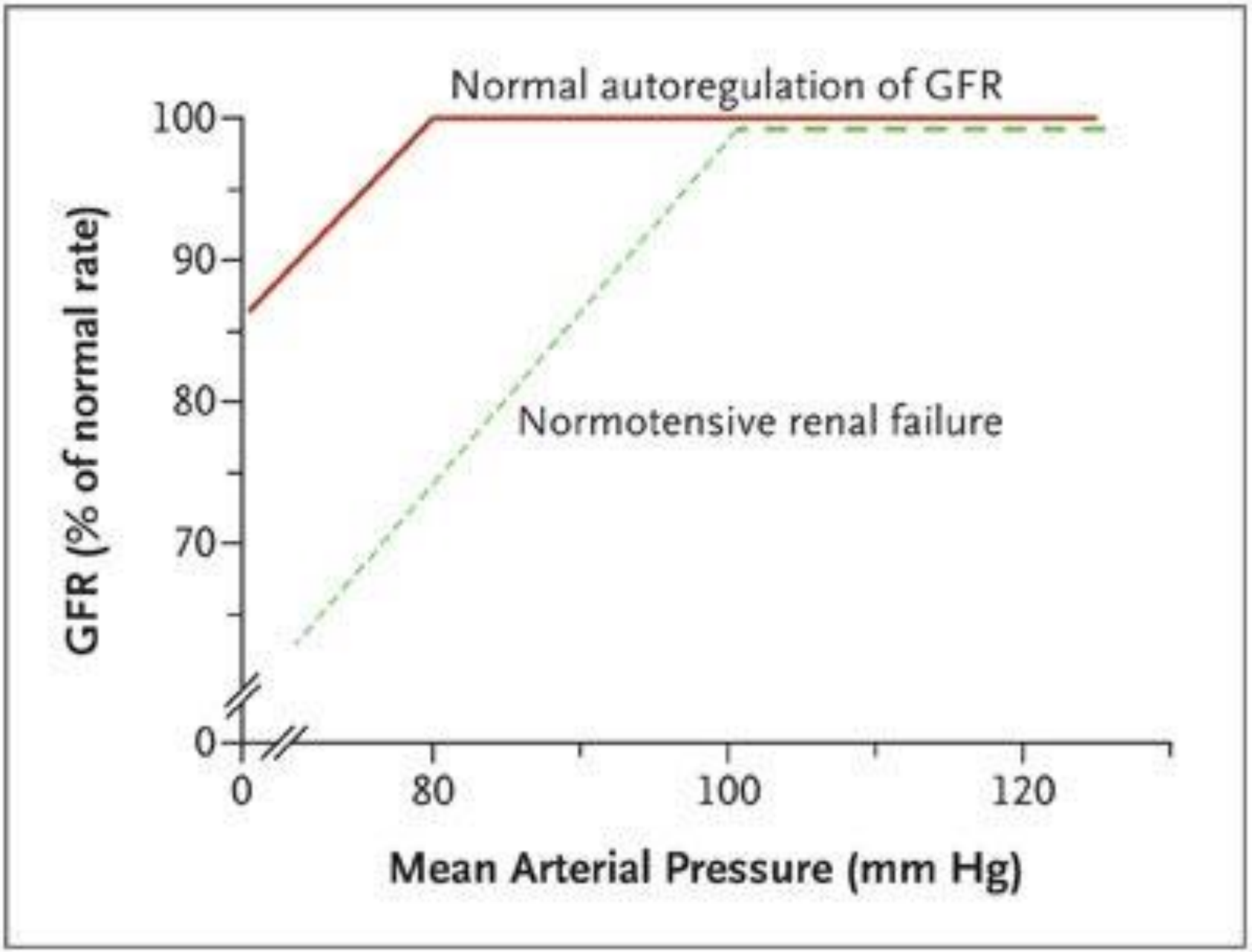
Miller, Schrier, Et al. Annals Int Med, 1978 Vol 89. p 47-50

66 yr twins w/ HTN go for a hike and become hypovolemic. Twin A is on lisinopril and Twin B is on amlodipine. Are they both equally likely to develop pre-renal AKI?

A. Yes
B. No, Twin A is more likely
C. No, Twin B is more likely

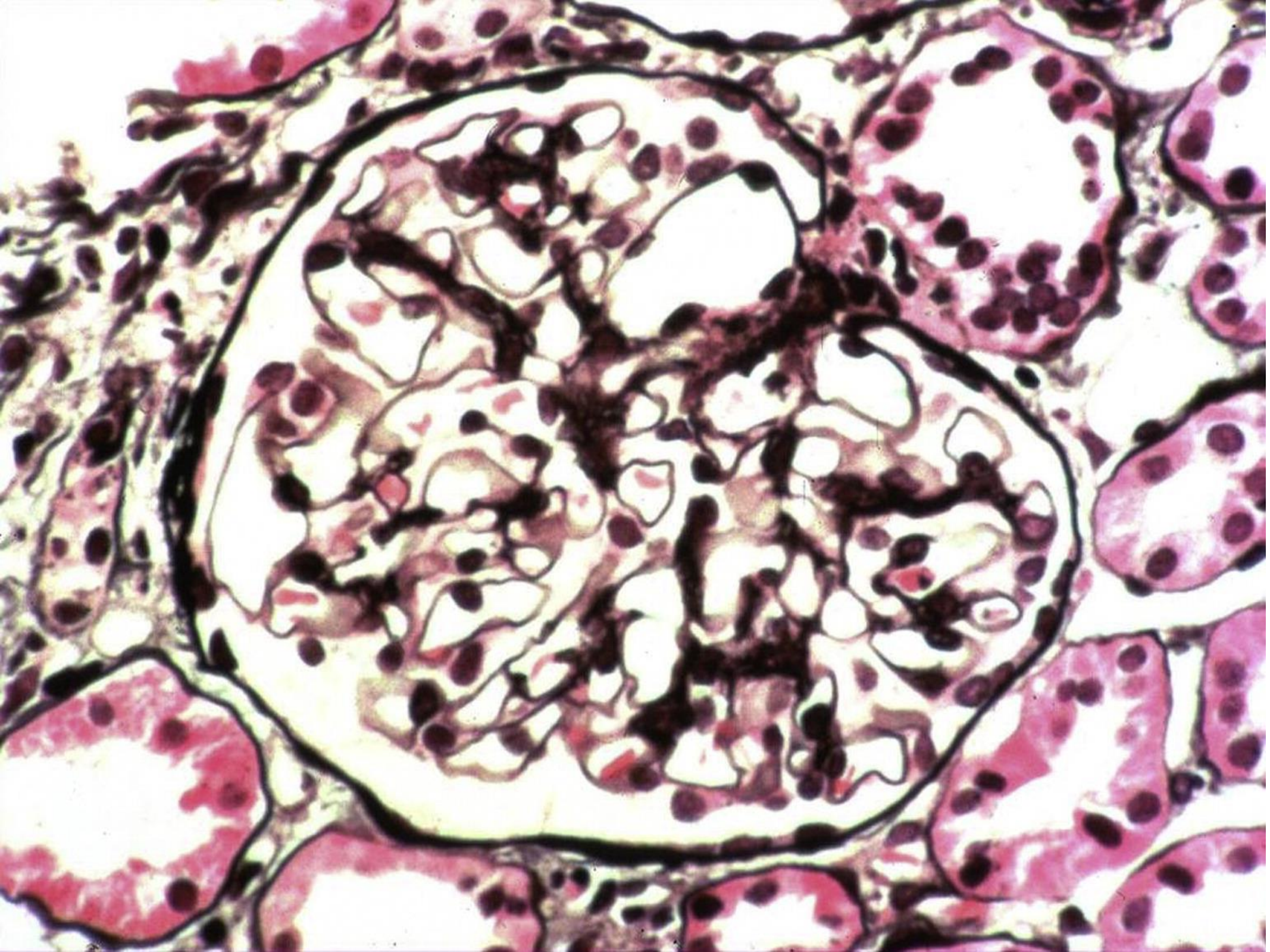

A Normal perfusion pressure
Arteriolar resistances
Afferent arteriole
Efferent arteriole
Glomerulus
Tubule
Normal GFR
B Decreased perfusion pressure
Increased vasodilatory prostaglandins
Increased angiotensin II
Normal GFR maintained


C Decreased perfusion pressure in the presence of NSAIDs
Decreased vasodilatory prostaglandins
Increased angiotensin II
Low GFR
D Decreased perfusion pressure in the presence of ACEI or ARB
Slightly increased vasodilatory prostaglandins
Decreased angiotensin II
Low GFR


Normal autoregulation of GFR
Normotensive renal failure
GFR (% of normal rate)
100
90
80
70
0
0
80
100
120
Mean Arterial Pressure (mm Hg)

What will you see if you biopsy the twin with pre-renal AKI?

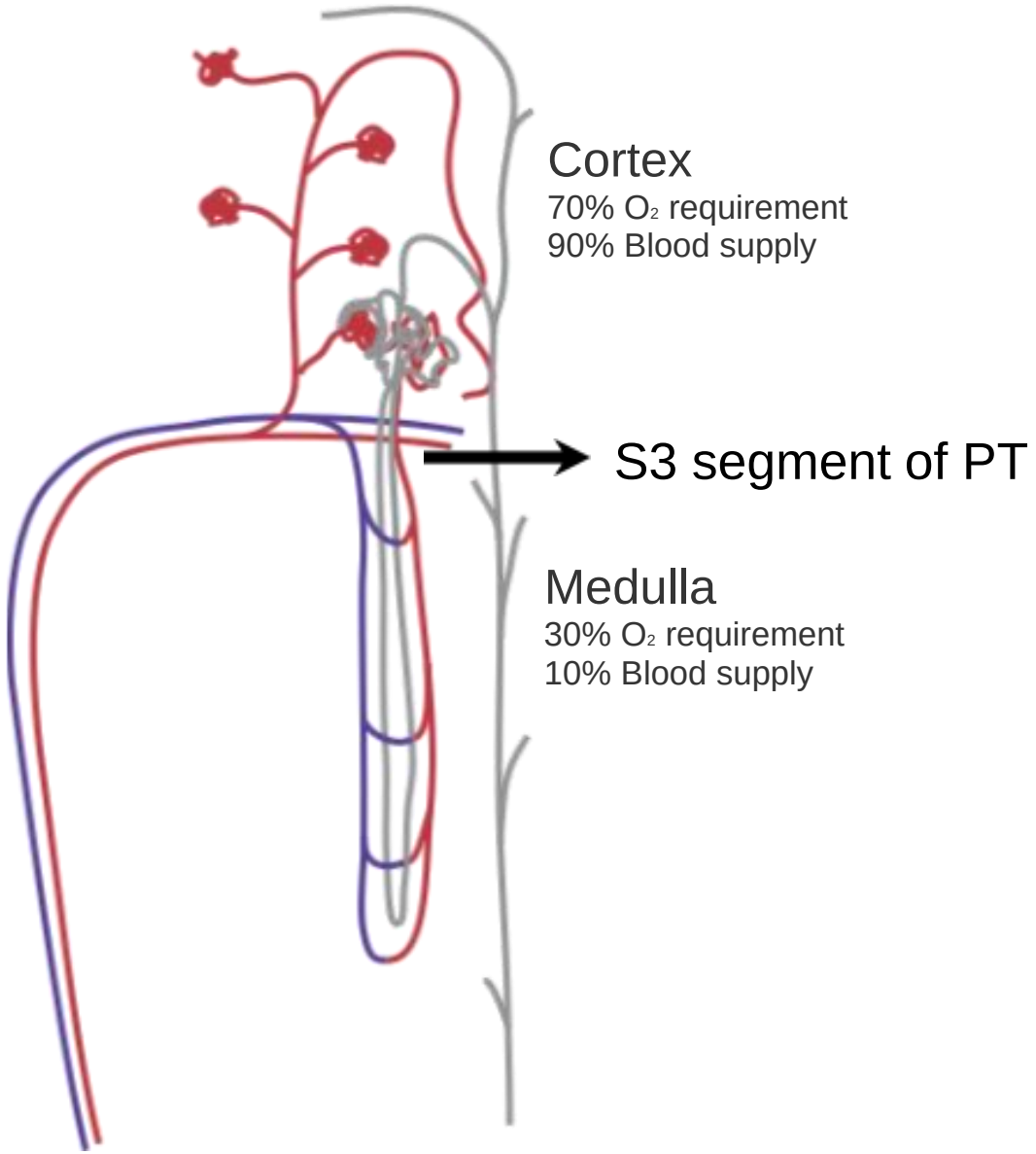
A. Normal looking kidney
B. Tubular damage
C. Glomerular damage
D. Afferent arteriolar vasodilatation

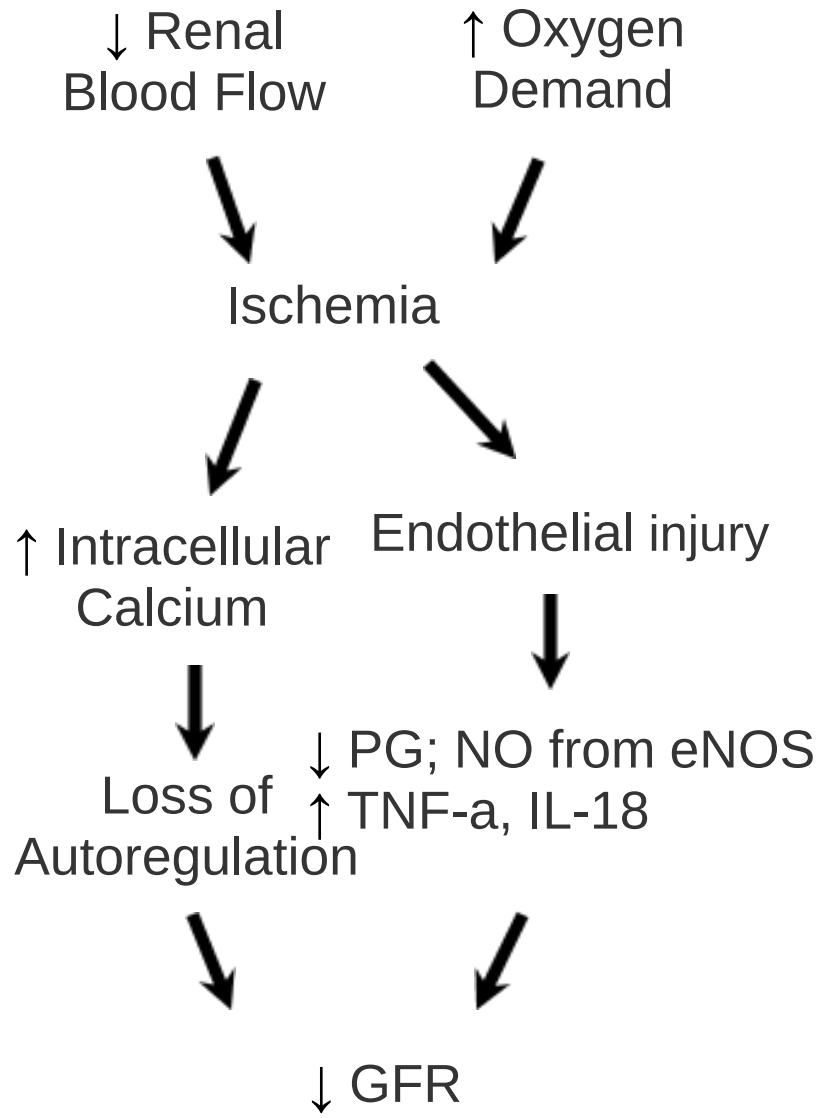


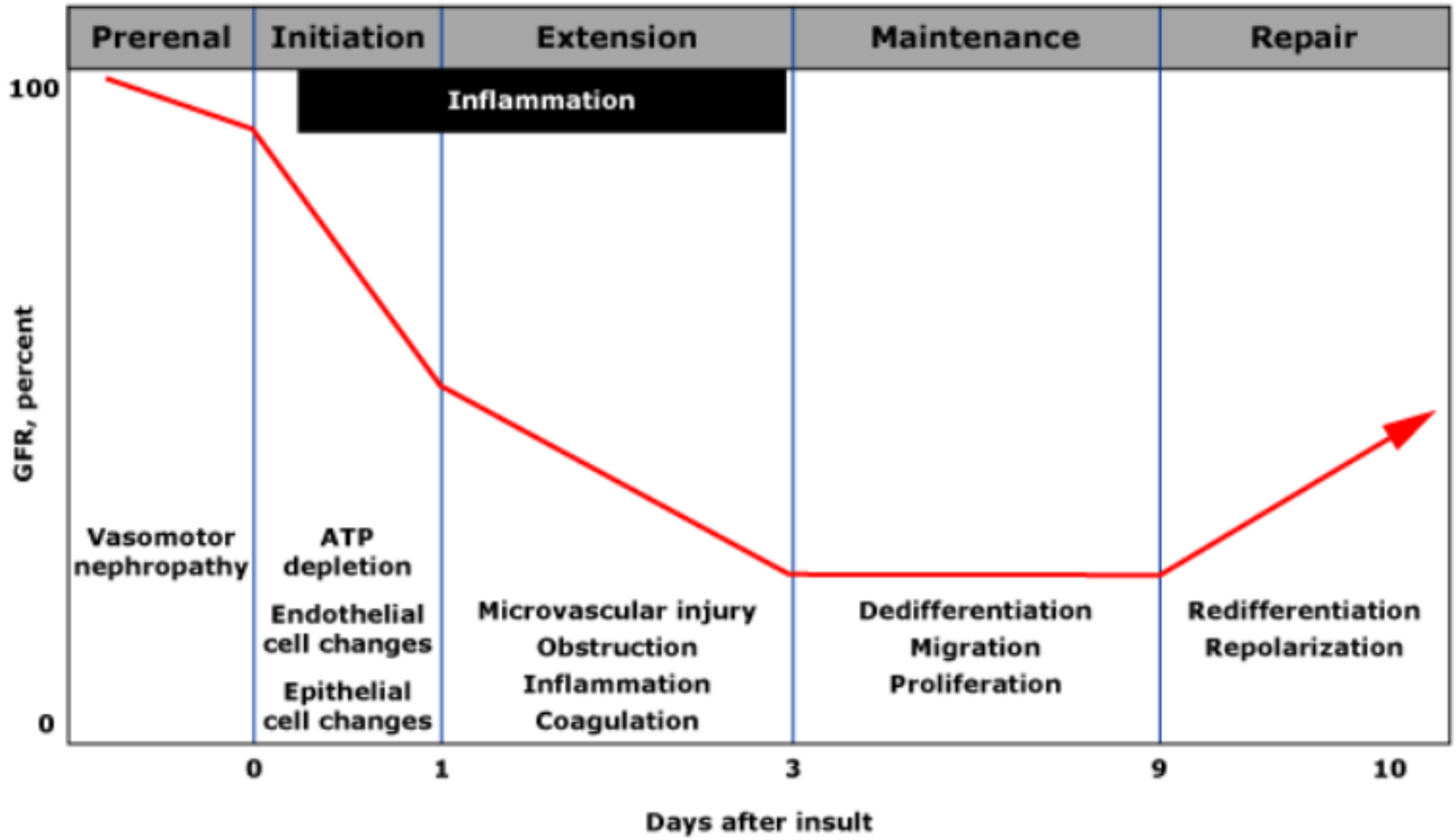
The twins don’t get re-hydrated and end up being hypovolemic for 72 hours.

Can they develop ATN?

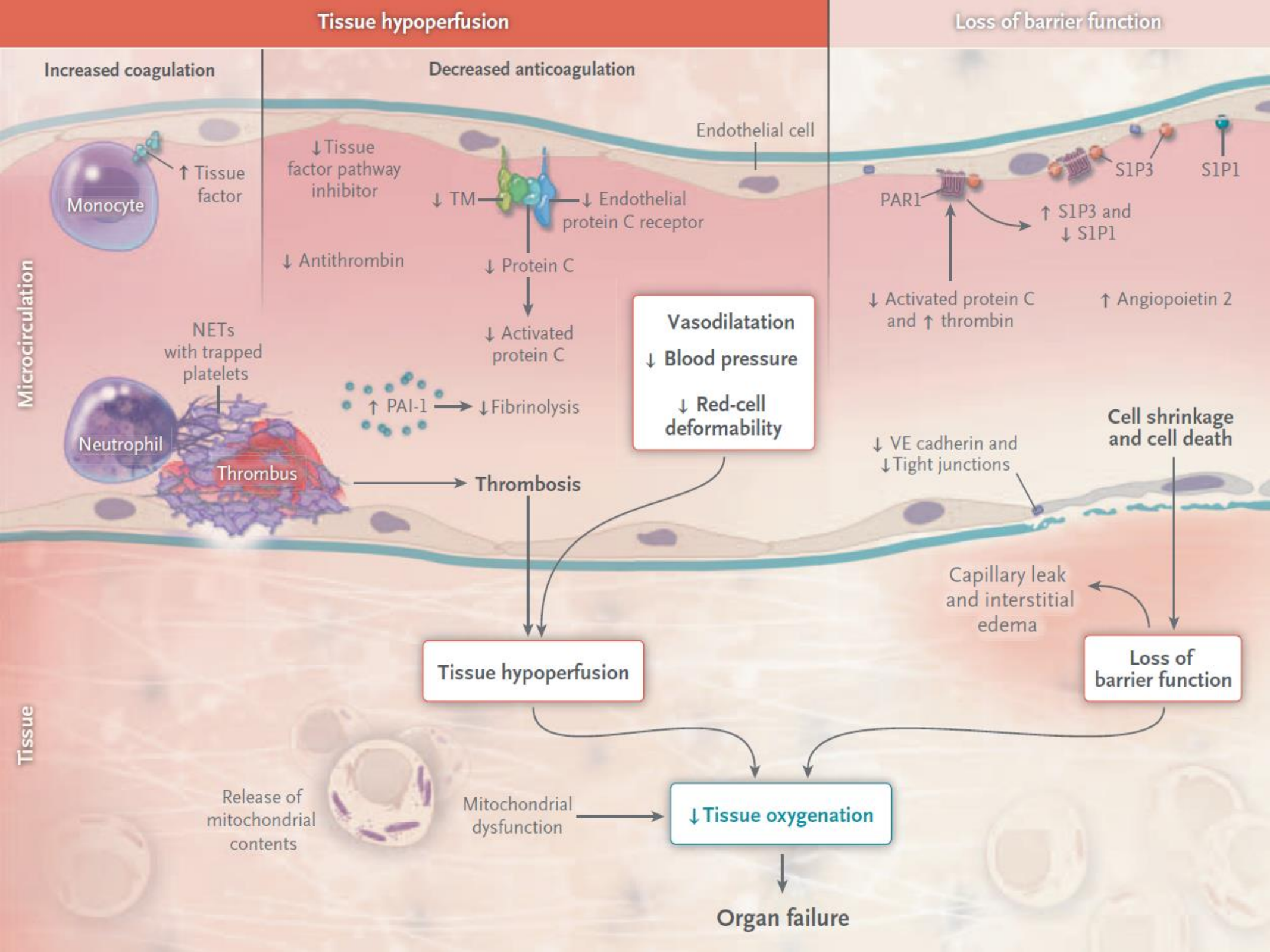
A. Yes
B. No

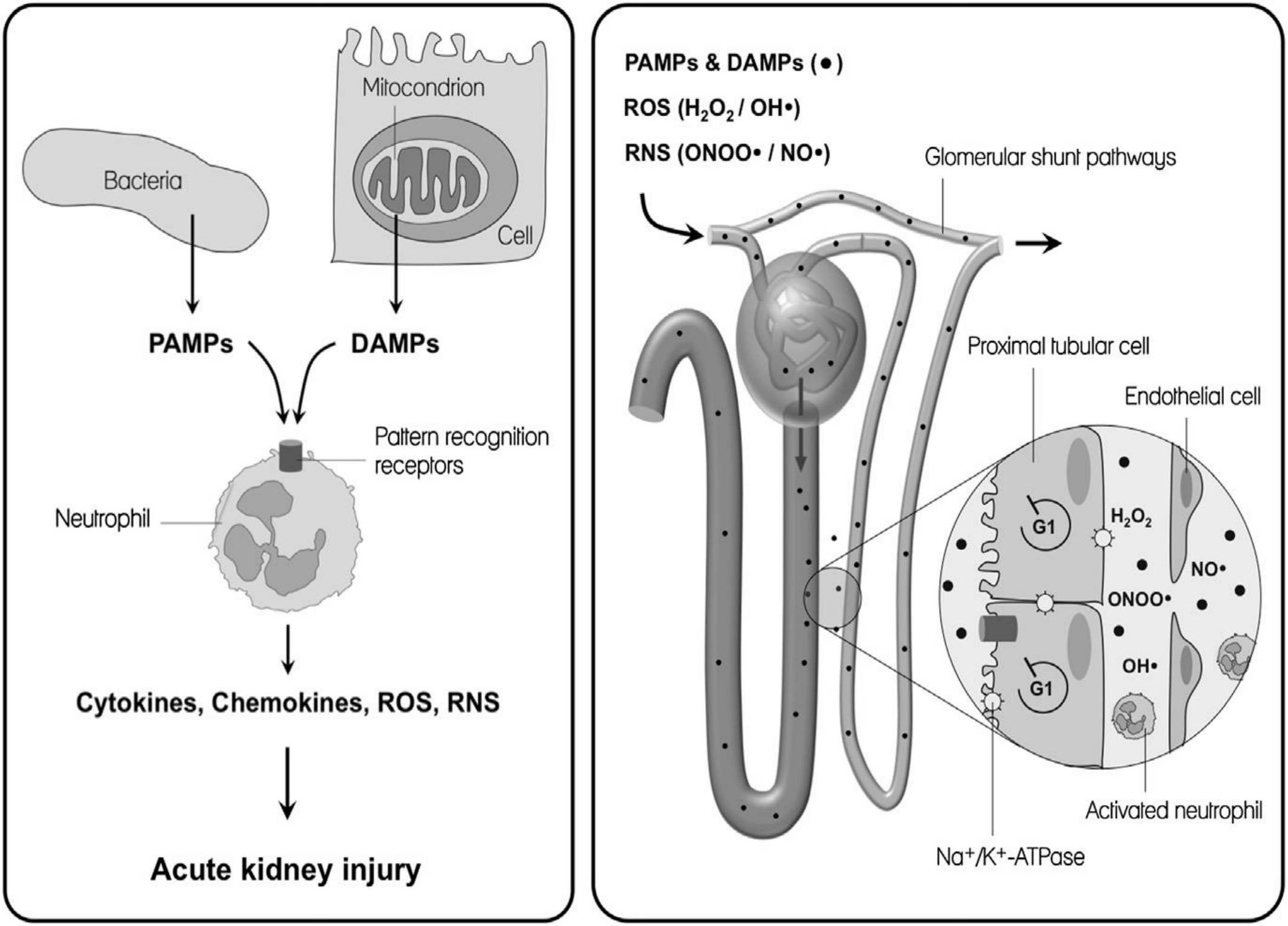

Cortex
70% O_2 requirement
90% Blood supply
S3 segment of PT
Medulla
30% O_2 requirement
10% Blood supply

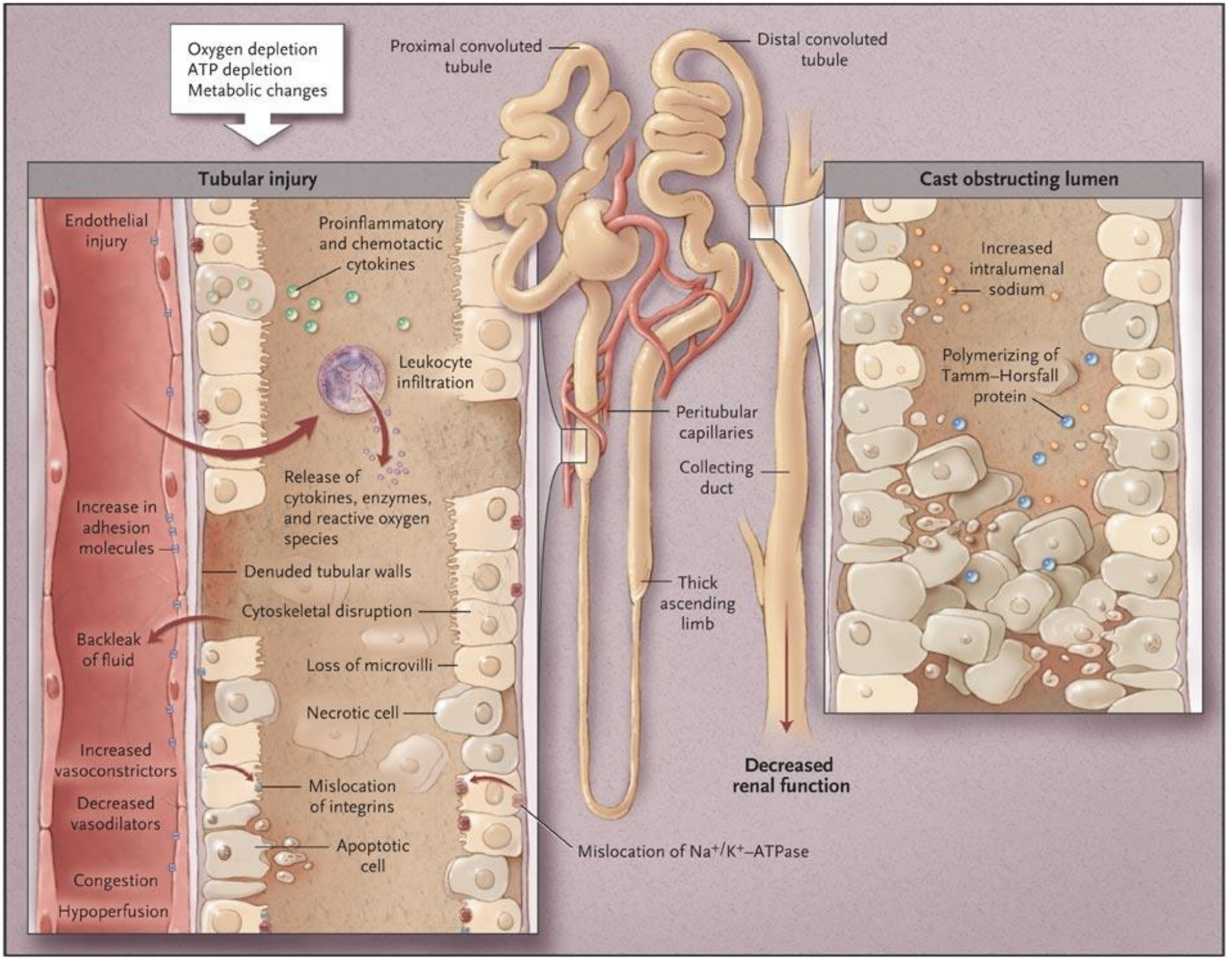

↓ Renal Blood Flow
↑ Oxygen Demand
Ischemia
↑ Intracellular Calcium
Endothelial injury
↓ PG; NO from eNOS
↑ TNF-a, IL-18
Loss of Autoregulation
↓ GFR

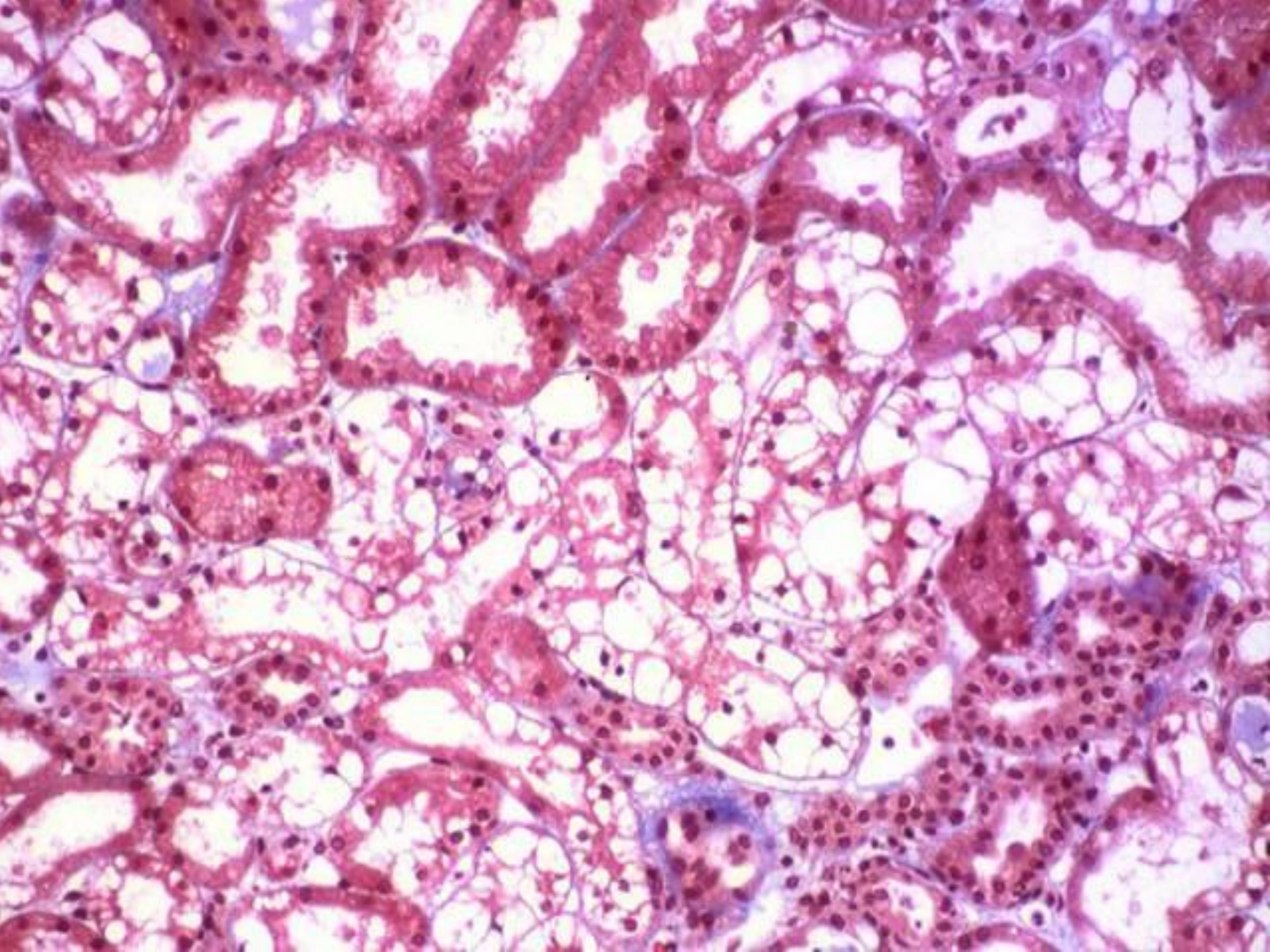


Adapted with permission from: Sutton, TA, Fisher, CJ, Molitoris, BA, et al. Microvascular endothelial injury and dysfunction during ischemic acute renal failure. Kidney Int 2002; 62:1539.


Tissue hypoperfusion
Loss of barrier function
Increased coagulation
Decreased anticoagulation
Microcirculation
Tissue
Monocyte
↑ Tissue factor
↓ Tissue factor pathway inhibitor
Endothelial cell
↓ TM
↓ Endothelial protein C receptor
↓ Antithrombin
↓ Protein C
↓ Activated protein C
PAR1
S1P3
S1P1
↑ S1P3 and ↓ S1P1
↓ Activated protein C and ↑ thrombin
↑ Angiopoietin 2
NETs with trapped platelets
Neutrophil
Thrombus
↑ PAI-1
↓ Fibrinolysis
Vasodilatation
↓ Blood pressure
↓ Red-cell deformability
Thrombosis
↓ VE cadherin and ↓ Tight junctions
Cell shrinkage and cell death
Capillary leak and interstitial edema
Tissue hypoperfusion
Loss of barrier function
Release of mitochondrial contents
Mitochondrial dysfunction
↓ Tissue oxygenation
Organ failure


Mitocondrion
Cell
Bacteria
PAMPs
DAMPs
Pattern recognition receptors
Neutrophil
Cytokines, Chemokines, ROS, RNS
Acute kidney injury
PAMPs & DAMPs (•)
ROS (H_2O_2 / OH•)
RNS (ONOO• / NO•)
Glomerular shunt pathways
Proximal tubular cell
Endothelial cell
G1
H_2O_2
NO•
ONOO•
OH•
G1
Activated neutrophil
Na^+/K^+-ATPase


Oxygen depletion
ATP depletion
Metabolic changes
Proximal convoluted tubule
Distal convoluted tubule
Tubular injury
Endothelial injury
Proinflammatory and chemotactic cytokines
Leukocyte infiltration
Release of cytokines, enzymes, and reactive oxygen species
Increase in adhesion molecules
Denuded tubular walls
Cytoskeletal disruption
Backleak of fluid
Loss of microvilli
Necrotic cell
Increased vasoconstrictors
Mislocation of integrins
Decreased vasodilators
Apoptotic cell
Congestion
Hypoperfusion
Peritubular capillaries
Collecting duct
Thick ascending limb
Mislocation of Na+/K+–ATPase
Decreased renal function
Cast obstructing lumen
Increased intralumenal sodium
Polymerizing of Tamm–Horsfall protein



25 yr male without any PMH goes for a hike. He presents to the ER w/ AKI (Cr 2).

The FeNa is pending.

On the UA, he has 6-10 granular casts/hpf

What's the likelihood ratio he has ATN?

A. 0.1
B. 2.3
C. 5.5
D. 9.7

Likelihood ratio (LR) of ATN vs pre-renal azotemia on the basis of the number of granular casts in urinary sediment

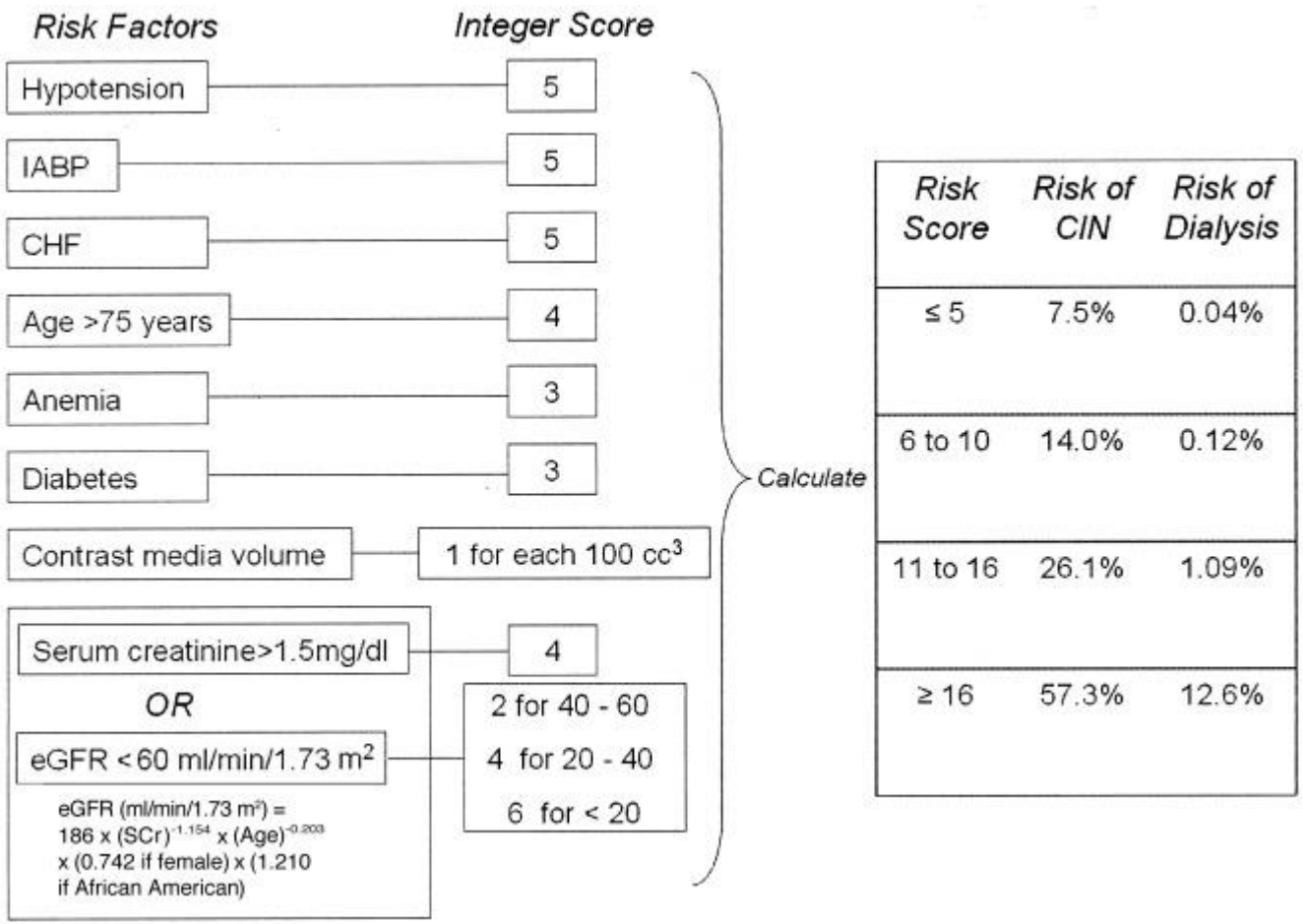
Granular casts/hpf	LR for ATN	LR for pre-renal
0	0.23	4.35
1-5	2.97	0.34
6-10	9.68	0.1

Clin J Am Soc Nephrol 4:691-693, 2009

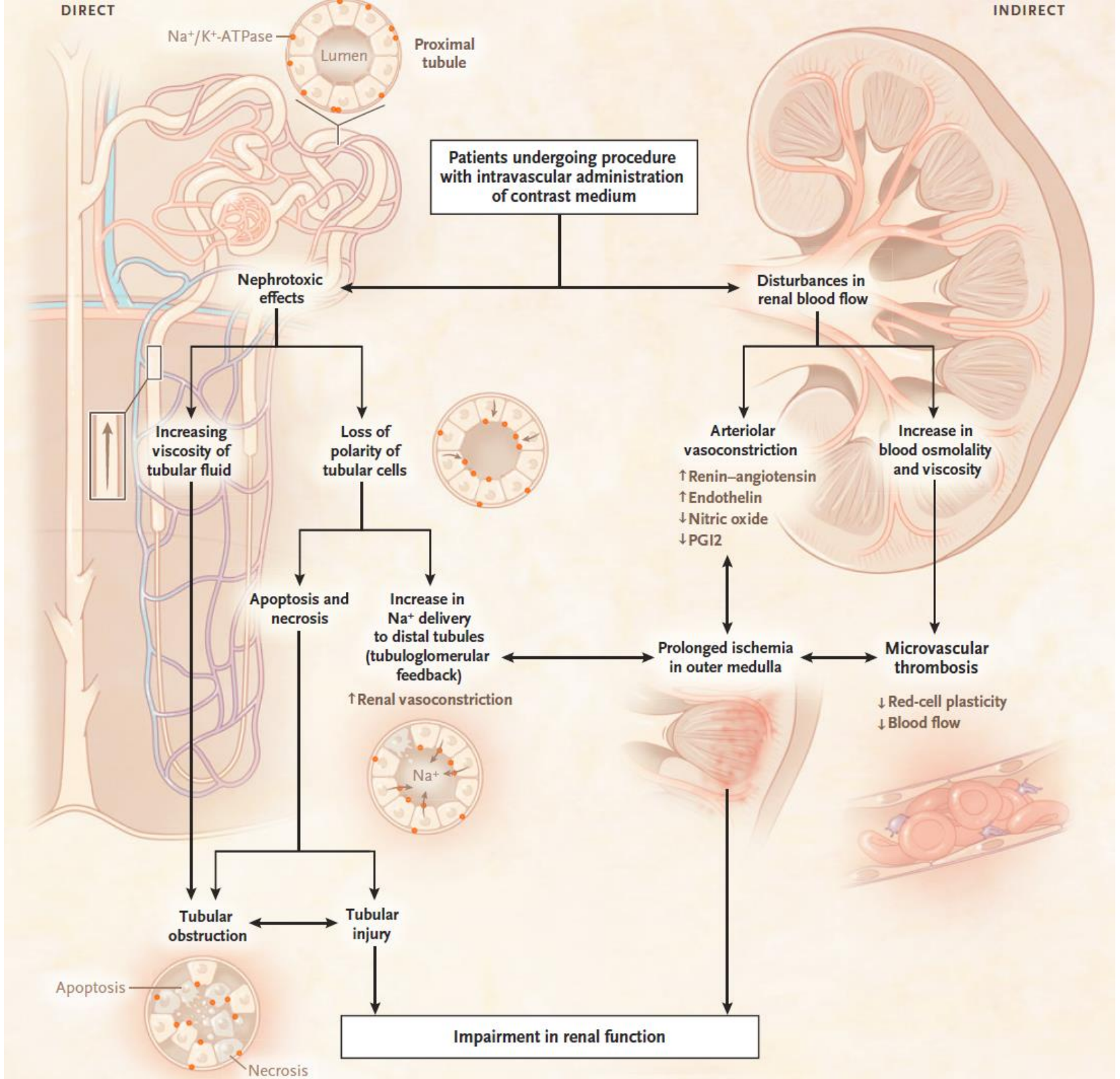
66 yr white male w/ DM, HTN, CAD, CKD stage 3, baseline Cr = 1.5, undergoes an elective coronary angiography

How likely is this patient to develop AKI needing dialysis?

A. 10%
B. 8%
C. 5%
D. < 1%
E. < 0.1%



Mehran et al. A Simple Risk Score for Prediction of Contrast-Induced Nephropathy After Percutaneous Coronary Intervention J Am Coll Cardiol 2004;44:1393-9.


DIRECT
INDIRECT
Na+/K+-ATPase
Lumen
Proximal tubule
Patients undergoing procedure with intravascular administration of contrast medium
Nephrotoxic effects
Disturbances in renal blood flow
Increasing viscosity of tubular fluid
Loss of polarity of tubular cells
Arteriolar vasoconstriction
↑Renin–angiotensin
↑Endothelin
↓Nitric oxide
↓PGI2
Increase in blood osmolality and viscosity
Apoptosis and necrosis
Increase in Na+ delivery to distal tubules (tubuloglomerular feedback)
↑Renal vasoconstriction
Prolonged ischemia in outer medulla
Microvascular thrombosis
↓Red-cell plasticity
↓Blood flow
Na+
Tubular obstruction
Tubular injury
Apoptosis
Necrosis
Impairment in renal function

What can you do to prevent contrast-associated acute kidney injury?

Pick all applicable answers

A. Use less volume of IV dye
B. Use iso-osmolar IV dye
C. Use 0.9% saline
D. Use N-acetylcysteine
E. Use dialysis after giving the IV dye

- Use iodixanol
- Use lower doses of contrast and avoid repetitive, closely spaced studies (eg, <48 hours apart)
- 0.9% NS X 1 mL/kg/hour for 6 to 12 hours preprocedure, intraprocedure, and for 6 to 12 hours postprocedure.

Mehran et al. Contrast-Associated Acute Kidney Injury. May 30, 2019
N Engl J Med 2019; 380:2146-2155

66 yr white male w/ DM, HTN, CAD admitted to an OSH w/ E Coli UTI, developed E Coli bacteremia and Shock (on vaso + levo) transferred to BUMC w/

- No UO x 12 hrs (despite IVF)
- Cr 4 (baseline 0.9)
- K 6.5

Should we start dialysis?

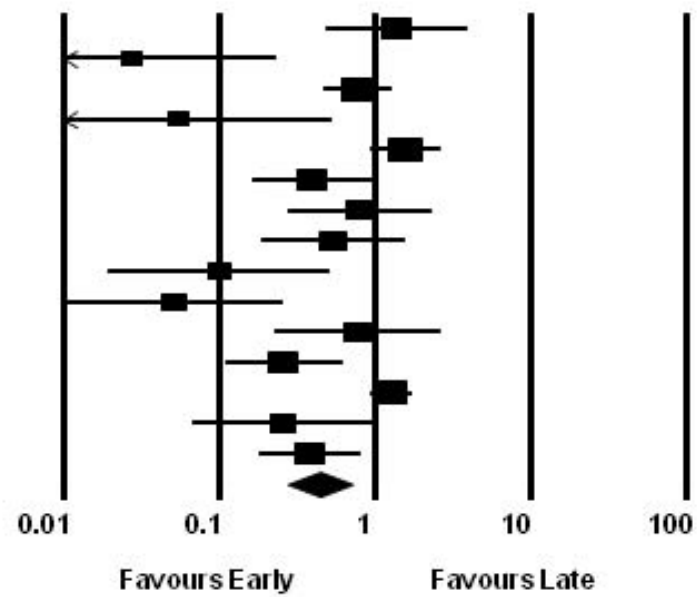
A. No
B. Yes

Accepted indications

- Refractory fluid overload
- Hyperkalemia (plasma potassium concentration >6.5 meq/L) or rapidly rising potassium levels
- Signs of uremia, eg pericarditis, neuropathy, or an otherwise unexplained AMS
- Metabolic acidosis (pH less than 7.1)
- Certain alcohol and drug intoxications
- Optimal timing based on BUN/Cr is unclear

Meta Analysis: All 15 studies

Study name	Subgroup within study	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bouman 2002	Mixed	1.375	0.487	3.884	0.601	0.548
Sugahara 2004	Surgery	0.028	0.003	0.231	-3.318	0.001
Liu 2006	Mixed	0.773	0.460	1.298	-0.974	0.330
Sabater 2008	Mixed	0.055	0.006	0.524	-2.520	0.012
Bagshaw 2010*	Mixed	1.563	0.933	2.619	1.697	0.090
Gettings 1999	Surgery	0.399	0.164	0.973	-2.019	0.043
Elahi 2004	Surgery	0.800	0.273	2.341	-0.407	0.684
Demirkilic 2004	Surgery	0.533	0.183	1.552	-1.154	0.249
Andrade 2007	Mixed	0.100	0.019	0.515	-2.752	0.006
Manche 2008	Surgery	0.051	0.010	0.256	-3.623	0.000
Iyem 2009	Surgery	0.778	0.229	2.644	-0.403	0.687
Shiao 2009	Surgery	0.260	0.110	0.614	-3.075	0.002
Bagshaw 2009 adj	Mixed	1.250	0.915	1.708	1.401	0.161
Wu 2007 adj	Surgical	0.259	0.068	0.988	-1.977	0.048
Carl 2010 adj	Mixed	0.380	0.177	0.816	-2.482	0.013
		0.446	0.276	0.723	-3.279	0.001



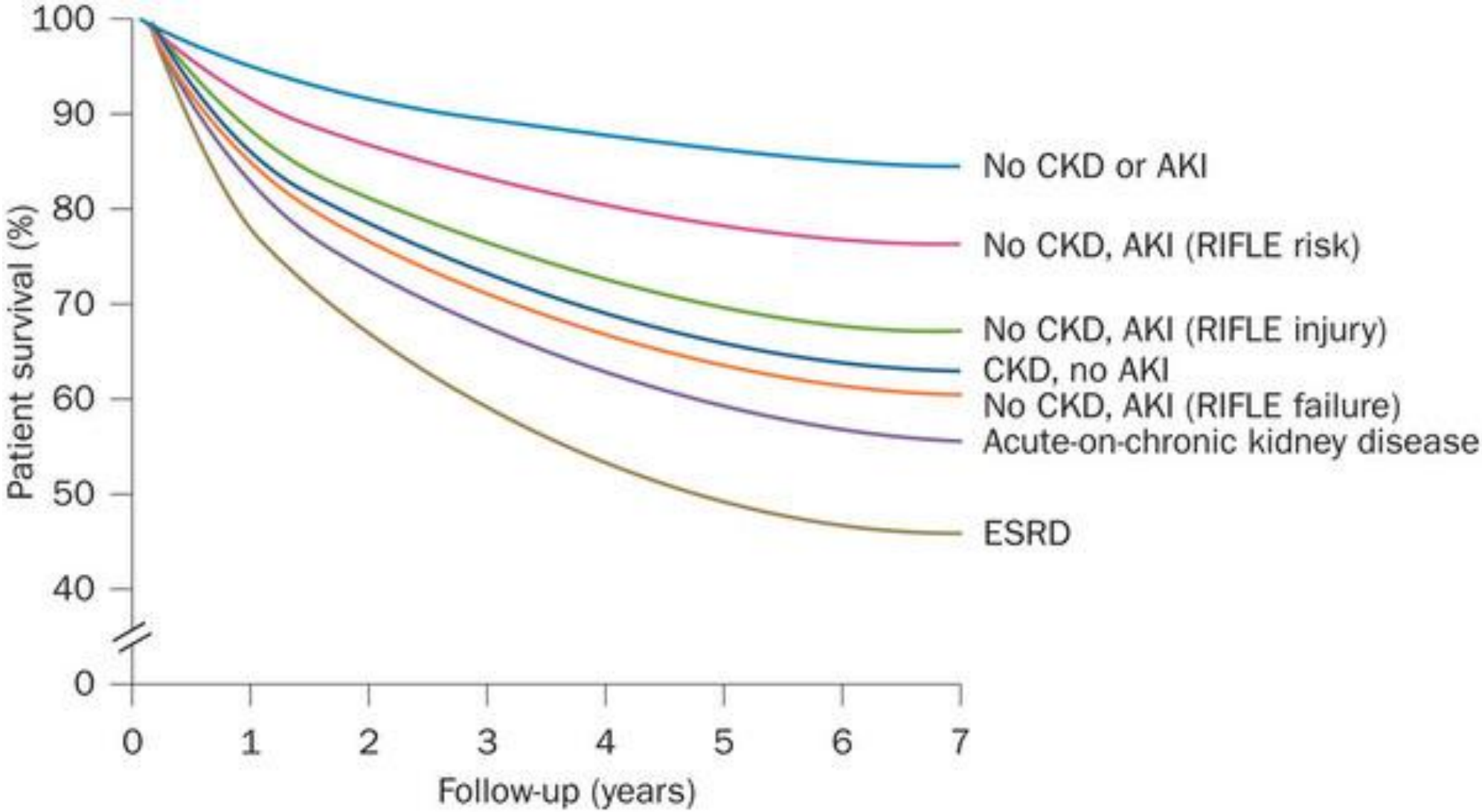
Meta Analysis

Karvellas, Constantine J., et al. "A comparison of early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury: a systematic review and meta-analysis." *Crit Care* 15.1 (2011): R72.

66 yr white male w/ DM, HTN, CAD, CKD stage 3, baseline Cr = 1.5, undergoes an elective coronary angiography and develops AKI. His Cr improves back to baseline at the time of discharge

How likely is he to survive 7 years after discharge (compared to controls)?

A. 100% (same as controls)
B. 90%
C. 80%
D. 60%



Wu et al, acute on chronic kidney injury at hospital discharge is associated with long-term dialysis and mortality, KI, Aug 2011

Questions?